Pre-B cell receptor-mediated activation of BCL6 induces pre-B cell quiescence through transcriptional repression of MYC.

Journal: Blood

Publication Year: 2011

Authors: Rahul Nahar, Parham Ramezani-Rad, Maximilian Mossner, Cihangir Duy, Leandro Cerchietti, Huimin Geng, Sinisa Dovat, Hassan Jumaa, B Hilda Ye, Ari Melnick, Markus Muschen

PubMed link: 21856866

Funding Grants: Dual targeting of tyrosine kinase and BCL6 signaling for leukemia stem cell eradication

Public Summary:
Initial cell surface expression of the pre-B cell receptor induces proliferation. After 2 to 5 divisions, however, large pre-BII (Fraction C') cells exit cell cycle to become resting, small pre-BII cells (Fraction D). The mechanism by which pre-BII cells exit cell cycle, however, is currently unclear. The checkpoint at the Fraction C'-D transition is critical for immunoglobulin light chain gene recombination and to prevent malignant transformation into acute lymphoblastic leukemia. Here we demonstrate that inducible activation of pre-B cell receptor signaling induces cell-cycle exit through up-regulation of the transcriptional repressor BCL6. Inducible activation of BCL6 downstream of the pre-B cell receptor results in transcriptional repression of MYC and CCND2. Hence, pre-B cell receptor-mediated activation of BCL6 limits pre-B cell proliferation and induces cellular quiescence at the small pre-BII (Fraction D) stage.

Scientific Abstract:
Initial cell surface expression of the pre-B cell receptor induces proliferation. After 2 to 5 divisions, however, large pre-BII (Fraction C') cells exit cell cycle to become resting, small pre-BII cells (Fraction D). The mechanism by which pre-BII cells exit cell cycle, however, is currently unclear. The checkpoint at the Fraction C'-D transition is critical for immunoglobulin light chain gene recombination and to prevent malignant transformation into acute lymphoblastic leukemia. Here we demonstrate that inducible activation of pre-B cell receptor signaling induces cell-cycle exit through up-regulation of the transcriptional repressor BCL6. Inducible activation of BCL6 downstream of the pre-B cell receptor results in transcriptional repression of MYC and CCND2. Hence, pre-B cell receptor-mediated activation of BCL6 limits pre-B cell proliferation and induces cellular quiescence at the small pre-BII (Fraction D) stage.